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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/425,742	10/22/99	KRAEMER	K 02481.1641

HM12/1115

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EXAMINER

WELLS, L

ART UNIT

PAPER NUMBER

1619

7

DATE MAILED:

11/15/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

## Office Action Summary

Application No.

09/425,742

Applicant(s)

KRAEMER ET AL.

Examiner

Lauren Q Wells

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

### Status

- 1) ☒ Responsive to communication(s) filed on 20 September 2000.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-29 is/are pending in the application.
- 4a) Of the above claim(s) 2-6 and 9-10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,7,8 and 11-29 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claims 1-29 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. § 119

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☒ All b) ☐ Some \* c) ☐ None of the CERTIFIED copies of the priority documents have been:
1. ☐ received.
2. ☒ received in Application No. (Series Code / Serial Number) 09/425,742.
3. ☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

### Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: \_\_\_\_\_

### DETAILED ACTION

Claims 1-29 have been presented for examination.

#### *Election/Restrictions*

Claims 1-29, drawn in Markush format, encompass multiple independent and patentably distinct inventions. Accordingly, a requirement to provisionally elect a single independent and patentably distinct species is made as provide for in MPEP § 803.02. It is noted that the claims encompass such final products as those set forth in Examples 1-5.

It is considered that a Markush-type claim encompassing such species is directed to multiple independent and patentably distinct inventions since the species are so unrelated and diverse that a reference anticipating one of the species would not anticipate or render obvious the other species. Further, the species are considered to be independent since they are unrelated in operation, one does not require the other for ultimate use, and the specification does not disclose a dependent relationship between them. Moreover, each of the stated species is considered to be patentably distinct from the others on the basis of its properties. Thus, the stated species are capable of supporting separate patents under 35 USC § 121.

Applicant is advised that a response to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election. By species is meant a single compound. The compound may be named in any of four ways (or any combination thereof): 1) according to the IUPAC standard, 2) by a pictorial representation of the compound, 3) by setting forth the specific chemical group that each variable of the Markush

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group represents, or 4) by naming a claim or an example which itself sets forth a single compound.

Since the instant claims are drawn to a composition of matter which contains more than one group of compounds, a single compound (as described above) should be elected for each group of compounds. It is not necessary to elect a single compound for groups of compounds which are inert and have no bearing on the patentability of the composition (e.g. it would not usually be necessary to elect which solvent or buffer system the composition will be associated with).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.C.C. § 103 of the other invention.

In the event that the Markush-type claims are not found to be allowable the examination of the claims presented will be limited to the Markush-type claims to the extent that they read on the elected species and claims directed solely to the elected species. The claims directed solely to the non-elected species will be held withdrawn from consideration. A requirement to elect a species has been held to be tantamount to a requirement for restriction under 35 USC § 121<sup>1</sup>.

During a telephone conversation with Sean Passino on 10/16/00 and 10/24/00 a provisional election was made with traverse to prosecute the invention of the compound of example 1. In terms of applicant's Markush variables, the sub-generic concept wherein the film

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<sup>1</sup> In re Herrick, 115 USPQ, Comm'r Pat.

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forming agent is vinylimidazolium methochloride/vinylpyrrolidone copolymer, wherein the plasticizer is polyethoxylated hydrogenated castor oil, wherein the sub-genus concept searched were all the compounds of formula (I), embracing the elected species, is deemed to represent a single invention concept. Consequently, those species which fall within said sub-generic concept are also being examined on their merits. Claims 1, 7, 8, 11-21 are considered generic to the species set forth above and are only being examined to the extent that they read upon the elected inventive concept (and any inventive concepts additionally examined) Affirmation of this election must be made by applicant in responding to the Office action. Claims 2-6 and 9-10 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected species.

***Claim Rejections – 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1, 7, 8, 11, 12, 13, 16, 17, 18, 22, 23, 24, 25, 26, 27, 28, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Flemming et al. (6,117,436), Claussner et al. (6,087,509) and Winters et al. (WO 95/30409) in view of Claussner et al (5,750,553) in further view of Bernardon (5,763,487), Bazzano (5,514,672), Lai (5,916,910), Ismail (5,541,220) and Galey et al. (WO 9221317), Dumats et al. (WO 9119701), Estradier et al. (EP 427625); USPTO-892 dated 10/26/00 and USPTO-1449 dated 10/22/99.

The instant claims are drawn to a composition for topical application with androgenic activity comprising a compound of formula (I) wherein the elected species is 4-[3-(4-hydroxybutyl)-4,4-dimethyl-2,5-dioxo-1-imidazolidinyl]-2-(trifluoromethyl)benzonitrile, a copolymer of vinylimidazolium methochloride and vinyl pyrrolidone as a surfactant, polyethoxylated hydrogenated castor oil as a plasticizer, and a solvent. The instant invention is also drawn to a process for making a product for the treatment of androgenic alopecia, hirsutism, seborrhea, or acne. The instant invention also discloses a process for the treatment of androgenic alopecia, hirsutism, seborrhea, or acne.

Claussner et al. teach (Col. 5, lines 59-60) 4-(3-(4-hydroxy-2-buten-1-yl)-4,4-dimethyl-2,5-dioxo-1-imidazolidinyl)-2-(trifluoromethyl)-benzonitrile, 4-(4,4-bis(fluoromethyl)-2,5-dioxo-3-(2-fluoroethyl)-1-imidazolidinyl)-2-(trifluoromethyl)-benzonitrile, 4-(2,5-dioxo-4,4-bis(fluoromethyl)-3-(4-hydroxy-2-buten-1-yl)-1-imidazolidinyl)-2-(trifluoromethyl)-benzonitrile, and 4-[2,4-dioxo-1-(4-hydroxybutyl)-1,3-diazospiro[4.5]decan-3-yl]-2-(trifluoromethyl)-benzonitrile and all possible racemic, enantiomeric and diastereoisomeric isomer forms as a medicament of formula (I), where formula (I) is a 1-imidazolidinyl-phenyl that is used (Col. 9, lines 35-46) for the treatment of cutaneous affections such as acne, hyperseborrhea, alopecia or hirsutism.

Flemming et al. teach a cosmetic care product for the skin and hair with two components. Flemming et al. teach (Col. 4, lines 66-67 and Col. 5, line 1) Luviquat® FC 905, a copolymer of vinylimidazolium methochloride and vinyl pyrrolidone, as the first component of the composition. Flemming et al. teach (Col. 10, lines 37-38) teach Cremophor® RH 410, which is polyethoxylated hydrogenated castor oil, as a solubilizer that is an additive in the composition.

Flemming et al. teach (Col. 7, lines 33-34) water, ethyl alcohol, propyl alcohol, and isopropyl alcohol as part of the second component.

Winters et al. teach a topical polymeric drug delivery system. Winters et al. teach (page 9, claim 1) a topical polymeric delivery system for administering a drug soluble in hydroalcoholic solutions which comprises a film forming polymer, a plasticizing agent, a crystallization inhibitor, a penetration enhancer, an alcoholic or hydroalcoholic solution, and a suitable drug. Winters et al. teach (page 4, lines 1-4) ethanol, isopropanol, and ethyl acetate as solvents. Winters et al. teach (page 4, lines 5, 8-10) methacrylates, celluloses, siloxanes, and copolymers of methacrylates, celluloses and siloxanes, preferably poly(2-hydroxy ethyl methacrylate) as film forming polymers. Winters et al. teach (page 4, lines 13, 16-18) Tween 20 (polyoxyethylene (20) sorbitan monolaurate) and Tweens of higher molecular weight, low molecular weight polyethylene glycols, glycerine or Labrasols (PEG-8-caprylic-capritriglyceride) as plasticizing agents.

Furthermore, Claussner et al. teach optionally substituted phenylimidazolidines and the pharmaceutical compositions containing them, their preparation process, and their use as medicaments. Claussner et al. teach (Col. 1, lines 24-50) an imidazolidine of general formula (I). Claussner et al. teach that  $Z_1$  and  $Z_2$ , which correspond to  $R_1$  and  $R_2$  of the instant invention, may be identical or different. Claussner et al. teach that  $Z_1$  and  $Z_2$  may be a cyano or a trifluoromethyl radical. Claussner et al. teach -A-B-, corresponding to "X" and "Y" of the instant invention, as an amide. Claussner et al. teach  $R_3$ , corresponding to  $R_4$  of the instant invention, as being chosen from the following radicals: a hydrogen atom; alkyl, alkenyl, alkynyl, aryl or arylalkyl radicals having at most 12 carbon atoms, these radicals being optionally

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substituted by one or more substituents chosen from halogen atoms and other radicals, such as hydroxy and hydroxyalkyl. Claussner et al teach (Col. 2, lines 9-10)  $R_4$  and  $R_5$  as identical or different and representing a hydrogen atom or an alkyl radical having 1-12 carbon atoms.

Claussner et al. teach (Col. 3, line 14-17) formula (I) in all possible racemic, enantiomeric and diastereoisomeric isomer forms, as well as the addition of salts. Claussner et al. teach (Col. 13, lines 58-60) formula (I) for the use as medicaments for (Col. 14 lines 1-2) the treatment of cutaneous affections such as acne, hyperseborrhea, alopecia or hirsutism. Claussner et al teach (Col. 14, lines 6-8) formula (I) can be used in combination with an inhibitor of  $5\alpha$ -reductase such as  $(5\alpha, 17\beta)$ -1,1-dimethylethyl-3-oxo 4-aza-androst-1-ene 17-carboxamide for the treatment of acne, alopecia or hirsutism. Claussner et al. teach (Col. 14, lines 10-11) that formula (I) can also be combined with a product stimulating hair growth such as Minoxidil for the treatment of alopecia.

Furthermore, Bernardon teaches pharmaceutically/cosmetically-active compounds that are useful for the treatment of mammalian skin and hair conditions such as acne, seborrhea, and alopecia. Bernardon teaches (Col. 8, line 19) diazoxide as an active additive of the composition.

Bazzano teaches compositions promoting hair growth for conditions such as alopecia. Bazzano teaches (Col. 21, lines 49-67) that diltiazem, flunarizine, nisoldipine, and verapamil may be used in the composition.

Lai teaches pharmacologically active agents and their uses. Lai teaches (Col. 3, lines 49-51) an agent that can be used to reduce cutaneous irritation and alopecia. Lai teaches (Col. 8, lines 51-54) captopril, fosinopril, and calcium channel blocking agents such as diltiazem, felodipine, nicardipine, nifedipine as pharmacologically active agents.



Ismail teaches agents for the treatment and protection of skin. Ismail teaches (Col. 8, example 24) pentoxifyllin as a component of a capsule used for treatment for conditions such as alopecia.

Estradier et al. teach salts of 2,4-diamino-alkoxy 3-sulph-oxy pyrimidinium hydroxide used in cosmetic compositions for preventing hair loss or promoting hair re-growth. Estradier et al. teach 2,4-diamino 6-(m-butyloxy) 3-sulphoxy pyridinium hydroxide.

Galey et al. teach compositions containing pyridine-1-oxide derivatives for combating hair loss and stimulating hair growth. Galey et al. teach 2,6-diamino-4-piperidinopyridine.

Dumats et al. teach 2,4-diamino triazine oxides(s) for prevention and treatment of hair loss. Dumats et al. teach 2,6-diamino-4-butoxy-2,3,5-triazine 1-oxide.

While Claussner et al. do not teach a copolymer of vinylimidazolium methochloride/vinyl pyrrolidone or polyethoxylated hydrogenated castor oil as part of the cosmetic composition, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the copolymer of vinylimidazolium methochloride/vinyl pyrrolidone and the polyethoxylated hydrogenated castor oil of Flemming to the composition of Claussner et al. because Flemming et al. teach that the copolymer and oil impart chemical and physical stability to the cosmetic composition during storage and use. Additionally, with regards to the optional additives, while Flemming et al. and Claussner et al. do not teach the specific additives described in the instant invention, it would have been obvious to one of ordinary skill in the art to have combined the additives of the prior art to the pharmaceutical compositions of Claussner et al. and Flemming et al. because Claussner et al. teach excipients incorporated into a composition with the active ingredient (formula (I)) and Flemming et al. teach that other known cosmetic

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additives, adjuvants and vehicle substances can be added to the preparation of the cosmetic care product. One of ordinary skill in the art would have been motivated to substitute the additives of Ismail, Lai, Bazzano, and Bernardon into the teachings of Claussner et al. and Flemming et al. so as to produce pharmaceutical compositions with enhanced ability to influence hair growth.

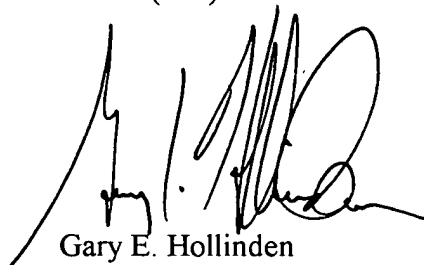
The claimed subject matter fails to patentably distinguish over the state of the art as represented by the cited references. Therefore, the claims are properly rejected under 35 U.S.C. § 103.

#### *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is (703) 305-1878. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary E Hollinden can be reached on (703) 308-4521. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

A handwritten signature in black ink, appearing to read 'Gary E. Hollinden', is written over a horizontal line.

Gary E. Hollinden  
Primary Examiner  
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